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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/321,987      | 05/28/1999  | JUDITH E. KIMBLE     | 960296.95386        | 7352             |

26734 7590 03/26/2002

QUARLES & BRADY LLP  
FIRSTAR PLAZA, ONE SOUTH PINCKNEY STREET  
P.O. BOX 2113 SUITE 600  
MADISON, WI 53701-2113

EXAMINER

SHUKLA, RAM R

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|----------|--------------|

1632

DATE MAILED: 03/26/2002

*do*

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/321,987

Applicant(s)

KIMBLE ET AL.

Examiner

Ram Shukla

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 03 January 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-10 and 13 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-10 and 13 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: *detailed action*.

### **DETAILED ACTION**

1. The request filed on 1-3-02 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/321,987 is acceptable and a CPA has been established. An action on the CPA follows.
2. Amendment filed 1-3-02 has been entered.
3. Amendments to claims 1 and 6-9 have been entered.
4. Claims 1-10 and 13 are pending.

### ***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-10 and 13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for identifying in a nematode a modulator of a gonadal cell migration activity of a protein, wherein the protein comprises a metalloprotease domain and a thrombospondin domain and wherein said nematode is a gon-1 mutant and lacks gonadal cell migration and comprises a gonadal distal tip cell, said method comprising: introducing in a nematode a polynucleotide comprising a nucleotide sequence encoding the protein operably linked to a promoter that specifically directs the expression of the nucleotide sequence in a distal tip cell and the protein is expressed in the gonadal distal tip cell, treating the nematode with at least one potential modulator of gonadal cell migration, observing in the treated nematode a change in the migration or shape of the developing gonadal cell attributable to modulation of the migration activity by the at least one potential modulator, wherein a change in the migration or shape of the developing gonadal cell results in the identification of the modulator, does not reasonably provide enablement for other embodiments. The

Art Unit: 1632

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

It is noted that applicants' new amendments to claims 1 and 6-9 do not obviate all the issues raised in the previous office actions. It is emphasized that the claimed invention is for identifying a compound that modulates the activity of a protein that directs the migration of a gonadal cell. The 1.132 declaration by the inventor Judith Kimble (filed 1-3-2002) is acknowledged. While the declaration is helpful in providing evidence that a human metalloprotease when introduced in a nematode has a distal tip cell migration-directing activity, it does not obviate the grounds of rejection since the assay as claimed is not for screening of proteins with metalloprotease and thrombospondin domains, rather it is for screening compounds that modulate the activity of the proteins. It is maintained that in the method of claim 1 one cannot distinguish that a modulator that affects the migration of the gonadal cell does so by modulating the activity of a metalloprotease enzyme since the role of other enzymes or proteins cannot be ruled out. The specification does not provide any direction as to how would an artisan have successfully identified such a modulator.

As noted in the previous office action of 12-13-00, claims recite only two steps, treatment of the nematode and observing the change in migration or shape of the developing gonadal cell, however, it is not clear whether only metalloproteases are the only enzymes/proteins responsible for gonadal cell migration. If not, the change in the migration or shape of the gonadal cell may result due to the effect of the compound on any protein other than the recited proteins and there is nothing in the method to indicate that the method would only target gon-1 or a protein that comprises a metalloprotease and thrombospondin. In other words, claimed method would not be able to indicate that a compound modulates the function of a protein as recited, since it cannot be excluded that the observed changes are not due to any other protein function modulation. For example, Chen and Stern (Trends in Genetics 14:322-327, 1998) noted that there

Art Unit: 1632

are multiple mechanisms that guide the migrations of the sex myoblasts in *C.elegans*, including attractive and repulsive ones, redundant sources of guidance information, and components that act in multiple aspects of sex myoblast migration. They further noted that the mechanism involves the action of many components known to function in other cell migrations, such as FGF receptor tyrosine kinase, RAS pathway components thought to modify the actin cytoskeleton (see the last paragraph in the last column on page 322). This clearly indicates that the gonadal cell migration is not only due to metalloprotease proteins and therefore treating any nematode with a modulator would not result in identifying a modulator of metalloprotease protein. In other words, the method as recited could not be practiced in a wild type animal since an artisan would not know whether the change in the migration of a gonadal cell was due to change in the activity of a metalloprotease or any other protein. Likewise, an artisan would not be able to practice in the context of the endogenous metalloprotease since there is no way of finding out as to whether a metalloprotease was affected in the method or any other protein was modulated by the compound. Furthermore, there is no guidance in the specification as to which promoter to express the protein from and in what tissue such that it is sufficiently close to the gonadal cell that the protein would be able to reach the gonadal tip cell and affect the gonadal cell migration. The specification does not provide any guidance as to how an artisan would have introduced a protein in a nematode such that it would reach a gonadal tip cell and modulate the migration of the cell.

It is noted that an artisan of skill would have required a great deal of experimentation to address the issues raised above and such an experimentation would have been undue at the time of the invention because the method of identifying a modulator of metalloprotease using a wild type nematode was not routine in the art at the time of the invention and the specification does not provide sufficient guidance for an artisan of skill to have practiced the claimed method. Accordingly, limiting the scope of the claimed invention to a method for identifying in a nematode a modulator of a gonadal cell migration activity of a protein, wherein the protein comprises a metalloprotease domain and a thrombospondin domain and

Art Unit: 1632

wherein said nematode is a gon-1 mutant and lacks gonadal cell migration and comprises a gonadal distal tip cell, said method comprising: introducing in a nematode a polynucleotide comprising a nucleotide sequence encoding the protein operably linked to a promoter that specifically directs the expression of the nucleotide sequence in a distal tip cell and the protein is expressed in the gonadal distal tip cell, treating the nematode with at least one potential modulator of gonadal cell migration, observing in the treated nematode a change in the migration or shape of the developing gonadal cell attributable to modulation of the migration activity by the at least one potential modulator, wherein a change in the migration or shape of the developing gonadal cell results in the identification of the modulator, is proper.

### ***Response to Arguments***

Applicant's arguments with respect to claims 1-10 and 13 have been considered but are moot in view of the new ground(s) of rejection.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-10 and 13 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite because it is unclear as to whether the protein recited in line 2 is an endogenous protein or has been introduced in the nematode exogenously.

Claim 6 is also vague and indefinite because it is unclear as to what would be considered "sufficiently close." Since the term "sufficiently" is a relative term, the metes and bounds of the invention are not clear.

Applicants have argued that "sufficiently close" is a well accepted claim format, however these arguments are not persuasive since there is no disclosure in



Art Unit: 1632

the specification which defines the term in relation to the instant invention.

Applicants have not provided any factual evidence to indicate that "sufficiently close" is an art accepted term in nematodes when expression of a protein is carried out in a cell and the protein is effectively transported to a tissue of action.

9. No claim is allowed.

When amending claims, applicants are advised to submit a clean version of each amended claim (without underlining and bracketing) according to § 1.121(c).

For instructions, Applicants are referred to

<http://www.uspto.gov/web/offices/dcom/olia/aipa/index.htm>.

Applicants are also requested to submit a copy of all the pending/under consideration claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for this Group is (703) 308-4242. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the Dianiece Jacobs whose telephone number is (703) 305-3388.

Ram R. Shukla, Ph.D.

*Ram R. Shukla*  
**RAM R. SHUKLA, PH.D**  
**PATENT EXAMINER**